

***AMENDMENTS TO THE CLAIMS***

This listing of the claims will replace all prior versions, and listings, of claims in the application.

***Listing of Claims:***

1. (Previously Presented) A method for promoting wound healing in a subject in need of such treatment comprising administering to the subject a wound-healing effective amount of a composition containing a wound-healing polypeptide selected from the group consisting of a first polypeptide comprising the amino acid sequence LKKTET (SEQ ID NO: 1) and having wound-healing activity and a second polypeptide comprising a conservative variant of said amino acid sequence and having wound-healing activity.
2. (Previously Presented) The method of claim 1, wherein the wound-healing polypeptide is thymosin  $\beta$ 4 or an isoform of thymosin  $\beta$ 4.
3. (Original) The method of claim 2, wherein the composition further contains an agent that stimulates the production of thymosin  $\beta$ 4 peptide.
4. (Original) The method of claim 3, wherein the agent is transforming growth factor beta (TGF- $\beta$ ).
5. (Previously Presented) The method of claim 1, wherein the wound-healing polypeptide is delivered systemically.
6. (Previously Presented) The method of claim 1, wherein the wound-healing polypeptide is delivered topically.
7. (Previously Presented) The method of claim 6, wherein the wound-healing polypeptide is contained in a topical formulation selected from the group consisting of a gel, cream, paste, lotion, spray, suspension, dispersion, salve, hydrogel and ointment.

8. (Previously Presented) The method of claim 1, wherein the wound-healing polypeptide is recombinant or synthetic.

9. (Withdrawn-Previously Presented) The method of claim 2, wherein the isoform of thymosin  $\beta$ 4 is at least 70% homologous to thymosin  $\beta$ 4 peptide set forth as SEQ ID NO:2.

10. (Withdrawn-Currently Amended) The method of ~~claim 9~~, wherein the isoform of thymosin  $\beta$ 4 is selected from the group consisting of: T $\beta$ 4<sup>ala</sup>, T $\beta$ 9, T $\beta$ 10, T $\beta$ 11, T $\beta$ 12, T $\beta$ 13, T $\beta$ 14 and T $\beta$ 15.

11. (Original) The method of claim 1, further comprising contacting the site of the wound with an agent which promotes wound healing.

12. (Withdrawn) The method of claim 11, wherein the agent is selected from the group consisting of IGF, IGF-I, IGF-2, IL-I, PDGF, FGF, KGF, VEGF, prothymosin  $\alpha$ , thymosin  $\alpha$  I or combinations thereof.

13. (Original) A method for promoting wound healing in a subject in need of such treatment comprising administering to the subject a wound-healing effective amount of a composition containing thymosin  $\beta$ 4 or an isoform of thymosin  $\beta$ 4.

14. (Currently Amended) The method of claim 13, wherein the composition comprises thymosin  $\beta$ 4, and further contains an agent that stimulates the production of thymosin  $\beta$ 4 peptide.

15. (Original) The method of claim 14, wherein the agent is transforming growth factor beta (TGF-b).

16. (Currently Amended) The method of claim 13, wherein the composition comprises thymosin  $\beta$ 4, and the thymosin  $\beta$ 4 is delivered systemically.

17. (Currently Amended) The method of claim 13, wherein the composition comprises thymosin  $\beta$ 4, and the thymosin  $\beta$ 4 is delivered topically.

18. (Currently Amended) The method of claim 17, wherein the composition comprises thymosin β4, and the thymosin β4 is contained in a topical formulation selected from the group consisting of a gel, cream, paste, lotion, spray, suspension, dispersion, salve, hydrogel and ointment.

19. (Currently Amended) The method of claim 13, wherein the composition comprises thymosin β4, and the thymosin β4 is recombinant or synthetic.

20. (Withdrawn) The method of claim 13, wherein the isoform of thymosin β4 is at least 70% homologous to thymosin β4 peptide set forth as SEQ ID NO:2.

21. (Withdrawn) The method of claim 13, wherein the isoform of thymosin β4 is selected from the group consisting of: T $\beta$ 4<sup>ala</sup>, T $\beta$ 9, T $\beta$ 10, T $\beta$ 11, T $\beta$ 12, T $\beta$ 13, T $\beta$ 14 and T $\beta$ 15.

22. (Original) The method of claim 13, further comprising contacting the site of the wound with an agent which promotes wound healing.

23. (Previously Presented) A method for promoting wound healing in a tissue comprising contacting the tissue with a therapeutically effective amount of a composition containing a wound-healing polypeptide selected from the group consisting of a first polypeptide comprising the amino acid sequence LKKTET (SEQ ID NO: 1) and having wound-healing activity and a second polypeptide comprising a conservative variant of said amino acid sequence and having wound-healing activity

24. (Previously Presented) The method of claim 23, wherein the wound-healing polypeptide is thymosin β4 or an isoform of thymosin β4.

25. (Original) The method of claim 23, wherein the contacting is *in vivo* in a subject.

26. (Original) The method of claim 23, wherein the contacting is *ex vivo*.

27. (Original) The method of claim 23, wherein the subject is a mammal.

28. (Original) The method of claim 27, wherein the mammal is human.

29. (Original) The method of claim 24, wherein the composition further contains an agent that stimulates the production of thymosin  $\beta$ 4 peptide.
30. (Original) The method of claim 29, wherein the agent is transforming growth factor beta (TGF- $\beta$ ).
31. (Original) The method of claim 29, wherein the agent is a mineral.
32. (Original) The method of claim 29, wherein the mineral is zinc.
33. (Previously Presented) The method of claim 23, wherein the wound-healing polypeptide is delivered topically.
34. (Previously Presented) The method of claim 23, wherein the wound-healing polypeptide is contained in a topical formulation selected from the group consisting of a gel, cream, paste, lotion, spray, suspension, dispersion, salve, hydrogel and ointment.
35. (Previously Presented) The method of claim 23, wherein the wound-healing polypeptide is delivered systemically.
36. (Original) The method of claim 23, further comprising contacting the site of the tissue with an agent which promotes wound healing.
37. (Withdrawn) The method of claim 36, wherein the agent is selected from the group consisting of IGF, IGF-I, IGF-2, PDGF, FGF, KGF, VEGF, prothymosin  $\alpha$ , thymosin  $\alpha$ 1 or combinations thereof.
38. (Original) The method of claim 23, wherein the tissue is selected from the group consisting of epidermal, eye, uro-genital, gastro-intestinal, cardiovascular, muscle, connective, and neural.
39. (Currently Amended) The method of claim 23, wherein the tissue is skin tissue.

40. (Previously Presented) The method of claim 23, wherein the tissue is an eye tissue.

41-52. (Canceled)

53. (Original) A method of promoting epithelial cell migration, comprising contacting an epithelial cell with a composition comprising thymosin  $\beta$ 4 or an isoform of thymosin  $\beta$ 4 .

54. (Currently Amended) The method of claim 53, wherein the composition comprises thymosin  $\beta$ 4, and the epithelial epithelial cell is a skin cell.

55. (Original) The method of claim 54, wherein the skin cell is a keratinocyte.

56. (Currently Amended) The method of claim 53, wherein the composition comprises thymosin  $\beta$ 4, and the epithelial cell is a corneal epithelial cell.

57. (Currently Amended) The method of claim 53, wherein the composition comprises thymosin  $\beta$ 4, and the contacting is *in vivo*.

58. (Currently Amended) The method of claim 57, wherein the composition comprises thymosin  $\beta$ 4, and the contacting is topical.

59. (Currently Amended) The method of claim 57, wherein the composition comprises thymosin  $\beta$ 4, and the contacting is systemic.

60. (Currently Amended) The method of claim 53, wherein the composition comprises thymosin  $\beta$ 4, and the contacting is *in vitro* or *ex vivo*.

61. (Original) The method of claim 53, wherein the composition is selected from the group consisting of a gel, cream, paste, lotion, spray, suspension, dispersion, salve, hydrogel, ointment, and a biocompatible matrix.

62-132. (Canceled)

133. (Previously Presented) The method of claim 1, wherein the wound is in a tissue selected from the group consisting of a skin tissue, a dermal tissue, an epidermal tissue, an

eye tissue, a cornea, a retina, a uro-genital tissue, a gastro-intestinal tissue, a cardiovascular tissue, a muscle tissue, a connective tissue, a neural tissue, a bone tissue, a cartilage tissue, a breast tissue, a central nervous system tissue, a pancreatic tissue, a liver tissue, a reticulo-endothelial system (RES) tissue and an endometrial tissue.

134. (Currently Amended) The method of claim 1, wherein the wound is present in a disease or condition selected from the group consisting of an arthritis, an osteoporosis, a musculo-skeletal disorder, a bum burn, an ulcer or an ulceration, a pressure ulcer, a diabetic ulcer, a skin lesion or disease, a neurological disease, a neurodegenerative disease, a nerve disease, a bone disease, a heart disease, an eye disease, corneal damage, retinal damage, skin damage, a cardiovascular disease, an ischemia, an atherosclerosis, a fibrotic disorder, a sclerotic disorder, a cancer and a cell proliferative disorder.

135. (Previously Presented) The method of claim 1, wherein the composition is administered by a route selected from the group consisting of an injection, a surgery, a catheter, a topical administration, a local injection, an inhalation, a systemic administration, an oral administration, an intranasal administration, an aerosol administration, an intravenous administration, an intraperitoneal administration, an intramuscular administration, an intracavity administration and a transdermal administration.

136. (Previously Presented) The method of claim 1, wherein the composition comprises a formulation comprising an excipient or a composition selected from the group consisting of saline, sterile water, a sodium chloride solution, lactated Ringer's intravenous, Ringer's dextrose, dextrose and sodium chloride, lactated Ringer's intravenous polyalkylene glycol, polyethylene glycol, vegetable oil, hydrogenated napthalene, lactide polymer, lactide/glycolide copolymer, polyoxethylene-polyoxypropylene, polyoxyethylene-9-lauryl ether, glycocholate and deoxycholate, phosphatidyl, phosphatidylglycerol, phosphatidylcholine, phosphatidylserine, phosphatidylethanolamine, sphingolipids, cerebrosides, gangliosides; phosphatidylcholine, dipalmitoylphosphatidylcholine, distearoylphosphatidyl-choline, injectable organic ester, ethyoleate, an alcoholic/aqueous solution, an alcoholic/aqueous emulsion, an alcoholic/aqueous suspension.

137-172. (Canceled)

173. (New) The method of claim 1 wherein said polypeptide is present in said composition at a concentration of at least about 0.01 ng/ml and up to about 60 micrograms per 300 microliter.

174. (New) The method of claim 13 wherein said polypeptide is present in said composition at a concentration of at least about 0.01 ng/ml and up to about 60 micrograms per 300 microliter.

175. (New) The method of claim 23 wherein said polypeptide is present in said composition at a concentration of at least about 0.01 ng/ml and up to about 60 micrograms per 300 microliter.

176. (New) The method of claim 53 wherein said polypeptide is present in said composition at a concentration of at least about 0.01 ng/ml and up to about 60 micrograms per 300 microliter.

177. (New) A method of treating or preventing tissue injury in a subject comprising administering to the subject a composition comprising a polypeptide comprising at least one of amino acid sequence LKKTET [SEQ ID NO:1] or a conservative variant thereof, thymosin  $\beta$ 4 (T $\beta$ 4), a T $\beta$ 4 isoform, a functional fragment of T $\beta$ 4 or a T $\beta$ 4 isoform having biological activity of T $\beta$ 4 or a T $\beta$ 4 isoform, T $\beta$ 4ala, T $\beta$ 9, T $\beta$ 10, T $\beta$ 11, T $\beta$ 12, T $\beta$ 13, T $\beta$ 14, T $\beta$ 15, gelsolin, vitamin D binding protein (DBP), profilin, cofilin, depactin, Dnasel, villin, fragmin, severin, capping protein, beta- actinin, or acumentin, wherein said tissue injury is associated with a wound healing disorder, a skin wound, an ulcer, a diabetic ulcer, a venus ulcer, a chronic ulcer, a burn, a muscular-skeletal disorder, arthritis, osteoporosis, neurological or nerve disease, neuron-degenerative disease, cardiovascular disease, ischemia, atherosclerosis, a tissue wound, tissue damage due to ischemia, ischemic brain disease, ischemic bone disease, ischemic heart disease, corneal tissue damage of the eye, retinal tissue damage of the eye, inflammation, epithelial tissue damage, tissue damage due to surgical procedures, tissue damage due to irradiation, tissue damage due to laceration, tissue damage due to toxic chemicals, tissue damage due to viral infections, tissue damage due to bacterial infections,

fibrotic disorder, sclerotic disorder, a disorder associated with under-expression of T $\beta$ 4 or a T $\beta$ 4 isoform, a recurrent wound, a tissue repair disorder, a fibrotic tissue disorder, an eye related wound, a deficiency in endometrial growth, endometrial tissue damage, a deficiency in placental growth, inability to maintain pregnancy, or a deficiency in endometrial-trophoblast interaction.

178. (New) A method of treating or preventing disease in a subject comprising administering to the subject an effective amount of a composition comprising an agent which increases the activity of, stimulates the production of, or up-regulates at least one of a polypeptide comprising amino acid sequence LKKTET [SEQ ID NO:1] or a conservative variant thereof, T $\beta$ 4, a T $\beta$ 4 isoform, a functional fragment of T $\beta$ 4 or a T $\beta$ 4 isoform having biological activity of T $\beta$ 4 or a T $\beta$ 4 isoform, T $\beta$ 4ala, T $\beta$ 9, T $\beta$ 10, T $\beta$ 11, T $\beta$ 12, T $\beta$ 13, T $\beta$ 14, T $\beta$ 15, gelsolin, vitamin D binding protein (DBP), profilin, cofilin, depactin, Dnasel, villin, fragmin, severin, capping protein, beta- actinin, acumentin, an actin-sequestering peptide, or an actin binding peptide, an actin-mobilizing peptide, or an actin polymerization-modulating peptide.

179. (New) A method of treating or preventing disease in a subject comprising administering to the subject an effective amount of a composition comprising an agent which decreases the activity of or down-regulates at least one of a polypeptide comprising amino acid sequence LKKTET [SEQ ID NO:1] or a conservative variant thereof, T $\beta$ 4, a T $\beta$ 4 isoform, a functional fragment of T $\beta$ 4 or a T $\beta$ 4 isoform having biological activity of T $\beta$ 4 or a T $\beta$ 4 isoform, T $\beta$ 4<sup>ala</sup>, T $\beta$ 9, T $\beta$ 10, T $\beta$ 11, T $\beta$ 12, T $\beta$ 13, T $\beta$ 14, T $\beta$ 15, gelsolin, vitamin D binding protein (DBP), profilin, cofilin, depactin, Dnasel, villin, fragmin, severin, capping protein, beta- actinin, acumentin, an actin-sequestering peptide, an actin binding peptide, an actin-mobilizing peptide, or an actin polymerization-modulating peptide.

180. (New) A method of promoting growth of a prosthetic tissue or organ, comprising administering a polypeptide to the prosthetic tissue or organ, the polypeptide agent comprising at least one of amino acid sequence LKKTET [SEQ ID NO:1] or a conservative variant thereof, T $\beta$ 4, a T $\beta$ 4 isoform, a functional fragment of T $\beta$ 4 or a T $\beta$ 4 isoform having biological activity of T $\beta$ 4 or a T $\beta$ 4 isoform, T $\beta$ 4ala, T $\beta$ 9, T $\beta$ 10, T $\beta$ 11, T $\beta$ 12, T $\beta$ 13, T $\beta$ 14,

T $\beta$ 15, gelsolin, vitamin D binding protein (DBP), profilin, cofilin, depactin, Dnasel, villin, fragmin, severin, capping protein, beta- actinin, or acumentin.

181. (New) A method of diagnosing a pathological state in a subject suspected of having pathology characterized by a disorder associated with T $\beta$ 4, comprising: obtaining a sample from the subject; detecting a level of T $\beta$ 4 in the sample; and comparing the level of T $\beta$ 4 in the sample to the level of T $\beta$ 4 in a normal standard sample.

182. (New) A composition for treating or preventing tissue injury in a subject comprising a polypeptide comprising at least one of amino acid sequence LKKTET [SEQ ID NO:1] or a conservative variant thereof, thymosin  $\beta$ 4 (T $\beta$ 4), a T $\beta$ 4 isoform, a functional fragment of T $\beta$ 4 or a T $\beta$ 4 isoform having biological activity of T $\beta$ 4 or a T $\beta$ 4 isoform, T $\beta$ 4ala, T $\beta$ 9, T $\beta$ 10, T $\beta$ 11, T $\beta$ 12, T $\beta$ 13, T $\beta$ 14, T $\beta$ 15, gelsolin, vitamin D binding protein (DBP), profilin, cofilin, depactin, Dnasel, villin, fragmin, severin, capping protein, beta- actinin, or acumentin; wherein said polypeptide is present in a carrier comprising an aerosol, alcoholic/aqueous emulsion, alcoholic/aqueous solution, alcoholic/aqueous suspension, aqueous physiological buffer suspension, aqueous solution containing deoxycholate, aqueous solution containing glycocholate, aqueous solution containing polyoxyethylene-9-lauryl ether, biocompatible and biodegradable lactide polymer, biocompatible and biodegradable lactide/glycolide copolymer, biocompatible and biodegradable polyoxethylene-polyoxypolyphylene copolymers, bioreasorbable polymer, controlled release matrix, dextrose and sodium chloride, electrolyte replenishers, electrolyte replenishers based on Ringer's dextrose, ethyl oleate, ethylene-vinyl acetate copolymer particles, fluid replenishers, glycholate, hydrogel, hydrogenated napthalenes, implantable infusion system, injectable organic esters, lactated Ringer's intravenous vehicles, lactose, lotion, nutrient replenishers, oil, oily solution, olive oil, osmotic pump, polyalkaline glycol, polyethylene glycol, porous material, propylene glycol, Ringer's dextrose, saline, salve, semi-solid suspension, sodium chloride solution, sustained release composition, tissue engineered construct or vegetable oil.